

Meili, R and R.A. Firtel (2002). Leading the way. *Nature Cell Biol.* 4:E171.

The ability to chemotax, that is, to sense and move in the direction of chemical signals, is a feature of a wide variety of eukaryotic cells. Chemotaxis is important for many biological responses, from the movement of leukocytes towards sites of infection or inflammation to the aggregation of *Dictyostelium discoideum* amoebae to form a multicellular organism. Recent work has firmly established the importance of the phosphatidylinositol 3-OH kinase (PI(3)K) pathway in mediating directional movement in response to chemoattractants. Insight into the mechanism that translates a shallow gradient of chemoattractant into cytoskeletal polarization and directional movement first came from work using *Dictyostelium* cells, and subsequently from studies with leukocytes and fibroblasts. These studies identified the importance of localized signalling by demonstrating that green fluorescent protein (GFP) fusions of a subfamily of pleckstrin homology (PH) domain-containing proteins, which specifically bind to the phosphoinositide products of PI(3)K, preferentially localized to the leading edge of chemotaxing cells. These findings strongly suggested that PI(3)K functions at the leading edge of the cell to mediate directional movement by using its products PtdIns(3,4,5)P₃ and PtdIns(3,4)P₂ as second messengers.